Vol. 75 August 1958 No. 8

ARCHIVES OF PEDIATRICS

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Bilateral Post-Traumatic Porencephaly — *Naomi Raskin, M.D.*

A Coccidioidal Fungicide — *Robert Cohen, M. D.*

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August 1958

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Some significant editorial highlights in September ARCHIVES will be an unusual journalistic feature—presentation of Dr. Hezekiah Beardsley's 1788 article on a "Pylorus" case, reviewed in ARCHIVES (1903) by Sir William Osler, with current analysis and commentary by Dr. Edward J. Donovan, St. Luke's Hospital (N. Y.). . . . Dr. Frederic Speer's "Food Allergy in Childhood" (known for his research in the field of allergies, Dr. Speer is the author of the recently-published book "Childhood Asthma") . . . an exceptionally interesting Conference on the timely problem of "staphylococcal infections" recently held at Roosevelt Hospital (N. Y.), Dr. Edmund Joyner III, Chief of Pediatrics, presiding; Dr. Heinz Eichenwald, Associate Professor of Pediatrics, Cornell University Medical College (N. Y.), guest.

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TUBERCULOSIS IN CHILDHOOD

Study on the Nature and the Pathogenesis of Some Pulmonary Changes Considered Particularly Characteristic

PHILIP SCHWARTZ, M.D.*

Warren, Pa.

In the course of the past decades, pathologic-anatomical, clinical, and particularly radiological observations defined a series of nosological entities, such as primary focus, primary complex, epituberculosis, middle lobe syndrome, etc., characterizing developmental processes and more-or-less stationary pulmonary modifications which were generally accepted in modern phthisiology. We will consider these conditions here, from the point of view of our experiences related to lymphonodogenous bronchial lesions and of our experimental investigations performed with R. Bieling.

I. EXPERIMENTAL BASIS FOR A CONCEPT OF PULMONARY TUBERCULOSIS IN MAN

Before the discovery of the paramount importance of lymphonodogenous tracheobronchial lesions, the concept of pulmonary tuberculosis was based on two groups of experiences: (1) Observations resulting from experimental pathology; (2) Findings gained through the help of clinical radiological observations.

Experiments disclosed that the susceptibility of an organism to tubercle bacilli is subjected to typical changes in the course of a tubercular infection. There are periods of the disease in which the inflammatory effect of the bacilli, or their toxins, is much more powerful than in a noninfected organism. In these cases, we deal with an *increased inflammatory susceptibility* (hypersensitivity) which may grow to such a level as to provoke anaphylactic shock (Koch, Behring, Römer, Bail, Rich, Schwartz and Bieling). In other stages of the tuberculous infection, however, the susceptibility of the organism to tubercle bacilli is considerably decreased and these agents become either completely unable to produce an inflammatory reaction (immunity), or they behave as avirulent

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germs, that is, they only induce indolent proliferative processes, inclining to heal (resistance) (Schwartz and Bieling).

In regard to the development of modern phthisiology, the most important result of *clinical radiological investigations* was the observation that during the course of pulmonary tuberculosis, infiltrates of considerable extension may develop in a very short time and may disappear without leaving any defects of the pulmonary tissue worth mentioning. (Eliasberg and Neuland, Redeker, Simon, Assmann). It was observed that these regressive (epituberculous) infiltrates may repeatedly appear in the course of chronic pulmonary tuberculosis and, indeed, that the tuberculous pulmonary disease generally develops in cycles, the climax of which is characterized by vehement infiltrative inflammatory processes and disintegration of the pulmonary parenchyma; while during the intervals only a torpid activity of the infection, or even a complete standstill of the disease prevails (Redeker).

Ranke had already endeavored to apply the concept of hypersensitivity and immunity observed in experimental investigations to characterize phenomena of tuberculous disease in man. Certain similarities to syphilis induced him to schematize the course of a tuberculous infection. According to Ranke, the first stage of pulmonary tuberculosis is characterized by the forming of a primary focus and by the involvement of regional lymph nodes; during the second stage, a hematogenic and lymphogenous contamination of the whole organism occurs, while following hypersensitivity, intensive pulmonary inflammation may develop. During the third stage, in which the organism resists and appears to be protected by antibodies, creeping inflammatory processes predominate, which spread only by direct contact through intracanalicular transport, restricted to one organ. Ranke developed his theory with the aid of Pirquet's allergy concept and Behring-Römer's experimental investigations. His conclusions were based on pathologic-anatomical observations in human tuberculosis. When, sometime later, Redeker, in systematic radiological investigations of individual cases of tuberculosis, recognized the sudden and repeated appearance of regressive pulmonary infiltrations and the cyclic course of chronic phthisis in general, he considered the infiltrative processes to be the expression of a hypersensitivity and explained the waning of morbid phenomena as the effect of immunity. Thus, increase of the inflammatory disposition (hypersensitivity) and immunity became, more and more, factors employed to characterize the clinical course of pulmonary tuberculosis.

The author, stimulated by Ranke's ideas and by Redeker's clinical observations, consecrated many years to the study of phthisiology from the standpoint of a general theory of infectious diseases. His investigations, performed with R. Bieling, concerning virulent and avirulent tuberculous infection in prepared and unprepared animals, as well as observations on inflammatory processes of different origin, permitted a pathogenetic, morphologic and clinical analysis of the pulmonary reactions occurring after experimental and spontaneous infection by tubercle bacilli.

At the time we temporarily terminated these studies, we were convinced that immunity and increasing sensitivity in the course of a tuberculous disease is of the greatest importance, not only in animals infected experimentally, but also in man. However, we remained dissatisfied, finding no explanation for the new exacerbative episodes of a chronic pulmonary tuberculosis. Specifically, we were unable to explain the occurrences which, in previously infected persons, though clinically healthy, induced the sudden appearance of circumscribed pulmonary infiltrations. Fortunately, it was possible later to fill these gaps. We know now that, between the cycles of chronic pulmonary tuberculosis, the tubercle bacilli persist in lymph nodes as seemingly harmless parasites for years and decades and that the onset of the clinically manifest episodes of pulmonary tuberculosis is induced chiefly by the discharge of exacerbated tuberculous lymph nodes into the tracheobronchial system.

Thus, we feel it imperative to harmonize our observations concerning the pathogenetic role of lymph node tuberculosis with the last results of investigations on immunity and sensitivity.

A. *Clinical Phenomena in Experimentally Induced Conditions and Their Pathogenetic Interpretation*

In experiments in which *avirulent* germs were given but once locally, intravenously and often intratracheally, we observed slowly developing changes in organs (Figs. 1, 2) which had no influence on the general condition of the animals and eventually healed completely. Manifestly, because of the innate resistance of the animals, the introduced agents were unable to produce noxious local or general inflammatory phenomena and were finally eliminated entirely.

In another experimental series a certain amount of *virulent* tubercle bacilli was injected only once locally, intravenously, and often intratracheally. After an initial state of well-being, mild

symptoms appeared which later suddenly became severe and were followed by a short period of prostration, characterized by dyspnea and a rapidly progressing deterioration ending lethally. (Fig. 3).

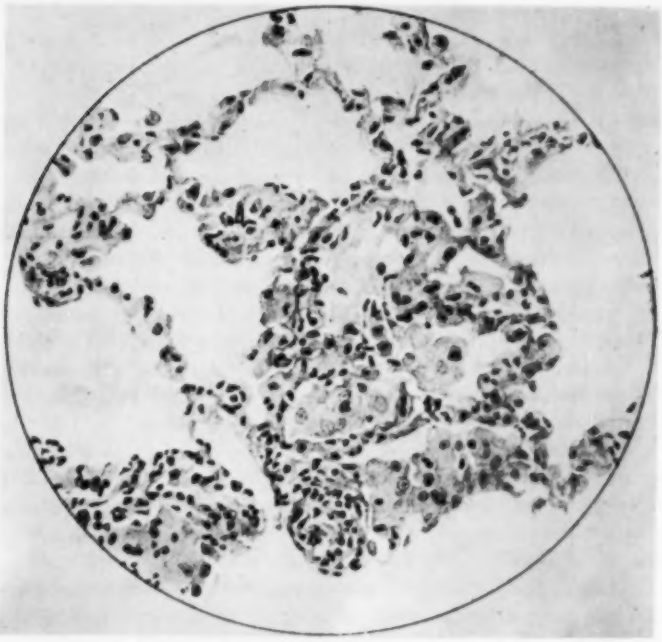

Fig. 1. Minute pulmonary foci in a rabbit sacrificed 21 days after the infection of the right testis with tubercle bacilli of the human type (which are avirulent for rabbits).

"a" . . . accumulation of alveolar histiocytes (containing tubercle bacilli!). No foci of granulation, no necroses were present. In animals of the same series, killed 8-12 weeks later, no pulmonary infiltrates were present.

Pathogenetic interpretation: The avirulent agents, spread everywhere in the body, induced only a mild preinflammatory proliferation of reticuloendothelial elements, because the innate resistance of the body prevented or reduced the inflammatory capacity of the tubercle bacilli. Intravenous or intratracheal superinfections, with virulent or avirulent tubercle bacilli, as well as killed tubercle bacilli or even their extracts introduced intravenously and intratracheally would, however, prove that the avirulent infection, 21 days after its administration, induced the development of both an important increase of the inflammatory susceptibility (sensitivity) and a very effective increase of the resistance to tubercle bacilli and their products.

A similar condition was observed in preinfected animals which had been subjected to an intravenous superinfection with virulent

or avirulent germs; many of these animals died in shock 24 to 48 hours after the superinfection, independently of the virulent or

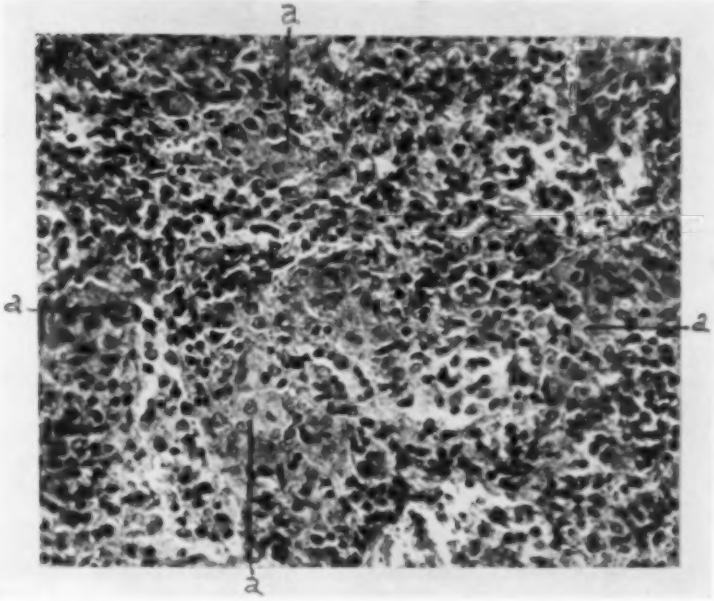

Fig. 2. Minute accumulations (*a*) of reticuloendothethelial cells in the spleen of a rabbit sacrificed 21 days after the infection of the right testis with tubercle bacilli of the human type (which are avirulent for rabbits). In animals of the same series, killed 10-12 weeks later, no splenic infiltrates were present.

Pathogenetic interpretation: The avirulent agents, spread everywhere in the body, induced only a mild preinflammatory proliferation of reticuloendothelial elements, because the innate resistance of the body prevented or reduced the inflammatory capacity of the tubercle bacilli. Intravenous or intratracheal superinfections, with virulent or avirulent tubercle bacilli, as well as killed tubercle bacilli or even their extracts introduced intravenously and intratracheally would, however, prove that the avirulent infection, 21 days after its administration, induced the development of both an important increase of the inflammatory susceptibility (sensitivity) and a very effective increase of the resistance to tubercle bacilli and their products.

avirulent nature of the bacilli used for the second infection (Fig. 4). However, other animals, which had been twice infected and survived the period of shock following the intravenous inoculation, recovered completely in a surprisingly short time, even in those cases in which the superinfection was accomplished with doses of

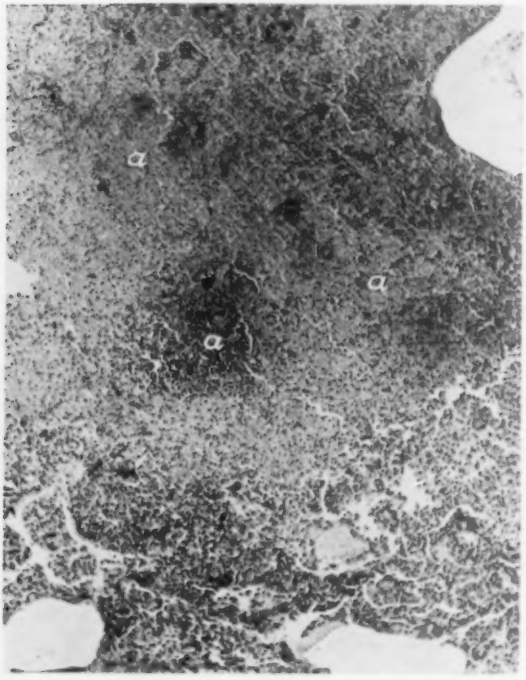

Fig. 3. Rabbit 3416, infected intravenously with bovine tubercle bacilli (which are virulent for rabbits) and found dead 43 days later, after displaying symptoms of prostration and shock. The autopsy disclosed a diffuse, caseous pneumonic infiltration (*a*) of both lungs, an extensive tuberculous involvement of all other organs, and changes, swelling of the spleen, typical necroses in liver, spleen, kidneys and heart muscle, which developed during the agonal period. These fresh lesions resembled alterations in preinfected animals, which perished in an anaphylactic shock *2 - 3* days after an intravenously administered superinfection.

Pathogenetic interpretation: The virulent tubercle bacilli could multiply without any inhibition during the first two to three weeks after the infection, because as yet there were no immune bodies present. After the third week, the inflammatory disposition (sensitivity) rapidly increased, provoking extensive infiltrations subjected to vast necroses. Simultaneously, effective immune bodies also appeared. The violent clinical symptoms before death, resembling shock, were the combined effect of the increasing inflammatory susceptibility and the spontaneous endogenous spread of the progressively increasing amount of living and disintegrated tubercle bacilli. Note the contrast between (1) the extensive destructive pulmonary involvement caused by virulent tubercle bacilli (Fig. 3); (2) the small, harmless, scattered pulmonary and splenic infiltrates following the infection with avirulent germs (Figs. 1 and 2); and (3) the predominantly cellular composition of the pulmonary condensation in a twice-infected animal (Fig. 7).

virulent agents powerful enough to kill control animals in a few weeks.

Fig. 4. Excessive, diffuse, bilateral pulmonary infiltration following superinfection with bovine (virulent) tubercle bacilli, intravenously administered (Rabbit 3396). The inflammatory susceptibility (sensitivity) of the animal was increased by a preceding infection of one testis with human (avirulent) tubercle bacilli. The superinfection was given 21 days after the infection of the left testis. The animal was sacrificed 8 days after the superinfection. Intravenously infected control animals of the same age showed almost no pulmonary changes; they perished, however, 4-6 weeks later of bilateral, massive caseous pneumonia.

Pathogenetic interpretation: The preparatory testicular infection caused both an increase of the inflammatory susceptibility and the appearance of a powerful immunity. When, 21 days after the testicular infection, the intravenous superinfection was administered, the spread of the agents immediately induced the development of an extensive inflammatory infiltration, which, up to the eighth day after the superinfection, almost entirely filled the lungs. However, thanks to the presence of an effective postinfectious immunity, many of the intravenously injected bacilli were destroyed immediately after their arrival in the lungs and others inhibited in their inflammatory capacity. Therefore, parallel animals of the same series which were not sacrificed only later showed typical healings and cleansing processes.

Very extensive, massive aspiration infiltrations, (Fig. 5) characterized by necroses, could be observed in prepared animals as

early as three days after superinfection administered intratracheally; these condensations often were transformed into giant cavi-

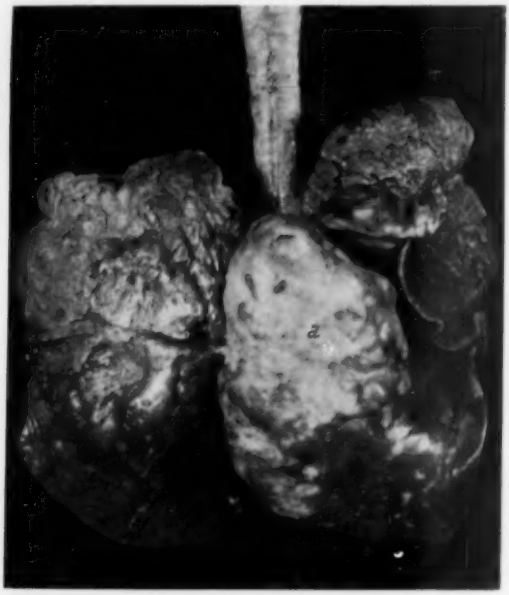

Fig. 5. Extensive aspiration infiltration of the right lower lobe of a previously infected rabbit (No. 2715), 3 days after intratracheal superinfection. In this case, the superinfection was administered with human (for rabbits avirulent) bacilli. Similar results were obtained, however, by intratracheal superinfections with virulent germs, with killed bacilli, or even with extracts of killed tubercle bacilli. The intratracheal administration of the same doses of human tubercle bacilli in nonpreinfected control animals produced no macroscopic pulmonary changes.

In this case, bovine bacilli were used for the preparatory testicular infection; in experiments, however, in which virulent germs or killed tubercle bacilli were employed for the preinfection, standard intratracheal superinfections had the same effect.

An interval of 21 days existed between the two infections. While control animals treated with the same doses of bovine bacilli only once perished without exception, twice-infected animals survived, displaying large cavities or extensive deforming pulmonary cicatrices.

ties a few weeks later (Fig. 6), during the period in which control animals had already perished.

In all these instances, the preinfection (administered chiefly into one testis) and the dissemination originating from the large

primary testicular focus increased the local and general inflammatory susceptibility (sensitivity) and induced the development of a more-and-more effective immunity. Then, three weeks after the preparatory treatment when the superinfection occurred, many of the newly introduced germs were immediately destroyed by the already very effective immunity (Bieling-Oelrichs' phenomenon), while, simultaneously, because of the concurrently prevailing extreme hypersensitivity, violent local and general inflammatory

Fig. 6. Giant pulmonary cavity of the right upper lobe following experimental aspiration infiltration in a sensitized animal, Rabbit No. 2676. Testicular preinfection with bovine tubercle bacilli (which are virulent for rabbits). Intratracheal superinfection (with human bacilli) 21 days later. Sacrificed 35 days after the superinfection.

processes were produced by the injection of the agents and the spreading of the products of their disintegration. The inflammatory susceptibility, after reaching a dangerous climax, in a relatively short time returns to its normal level, while the immunity

remains effective for a long time reducing the inflammatory capabilities of genuinely virulent germs. Therefore, animals which survive the shock period display only changes characterized by a healing tendency, just as in infections with avirulent bacilli (Fig. 7).

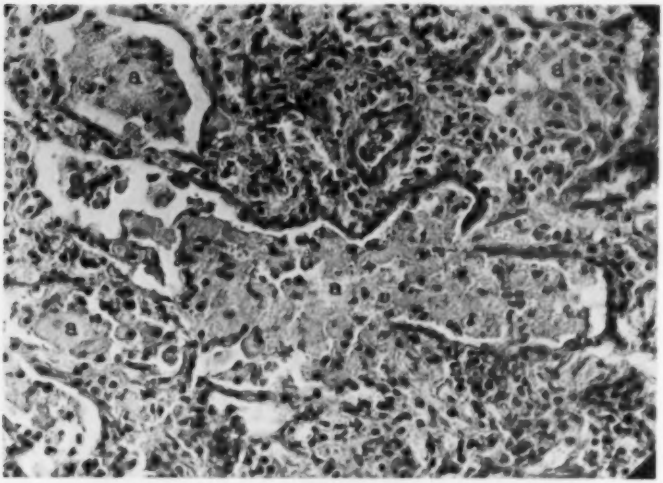

Fig. 7. Microscopic aspect of an experimentally produced "regressive" (rubber eraser-like) pulmonary infiltrate of specific origin. (Rabbit No. 2213). Testicular preinfection was administered with tubercle bacilli of the human strain (which are avirulent for rabbits). An intravenous superinfection with a fatal dose of bovine type tubercle bacilli was given 21 days later. The rabbit survived the shock period typical of twice-infected animals and died 25 days after the superinfection. The pulmonary changes were characterized by the accumulation (*a*) of alveolar histiocytes in the acini ("desquamative pneumonia"); very few necroses. Many other animals of this series survived, displaying progressive healing of the pulmonary disease. Control animals intravenously infected only once, however, perished without exception of massive caseous pneumonia within four to seven weeks.

These observations on twice-infected animals also permit the interpretation of processes developing after a single inoculation with virulent germs. We interpreted these changes in the following way: The introduced agents produced, immediately after their dissemination, inflammatory processes, the intensity of which increased with the progressively growing number of the germs. However, during the same time, the inflammatory susceptibility (sensitivity) of the involved organs also increased to such a degree that a lethal general reaction was produced by the microbes,

which by this time were very numerous and disintegrating because of the simultaneously developed immunity.

Radiological registration of our experimental observations permitted us to compare them directly with pulmonary tuberculosis in man. Extensive radiological condensations, which in prepared animals appeared within 24 to 48 hours after an intravenous or intratracheal superinfection, impressed us very strongly. These condensations grew during the first two or three weeks after the superinfection, and regressed in the course of a few months (Figs. 8*a* and 8*b*). Convincing and of direct clinical interest also were *experimental ocular infections* performed by Dr. E. Metzger with our standard doses; the rapid development, the initial increase, and then the regression of intraocular infiltrates induced by superinfection could be followed microscopically in the living animals (Fig. 9).

After having observed histologically, in joint investigations, that tubercle bacilli in fresh pulmonary infiltrations of superinfected animals disappear as early as 24 to 48 hours after the intravenous injection, Bieling also found a method of following this cleansing process bacteriologically. He prepared the animals by introducing a considerable amount of killed bacilli into one testis.* The superinfection was administered by the intravenous injection of a lethal dose of virulent (bovine) bacilli. It could be observed that in the lungs of prepared animals during the first hours after the superinfection, many more tubercle bacilli had gathered than in unprepared controls.** The large number of the bacilli soon decreased, however, and eventually the lungs contained no living agents or only a scattered few capable of proliferation (Bieling-Oelrichs' phenomenon).***

As emphasized in earlier publications, all clinical, pathological and anatomical conditions we experimentally produced occur also in tuberculous patients. Reversible pulmonary condensations in patients show exactly the same histologic structure as in our corresponding experimental observations. On the other hand, Redeker and Walter, as well as Ameuille and associates, as early as 1929 and

*Bieling chose killed bacilli for the preparatory treatment in order to leave no doubt concerning the origin of germs found in the blood after the superinfection.

**Freund and Angevine observed that in immunized animals, during the first hours following an injection into the skin, more bacilli were present in the skin, than in that of controls.

***Rist and Rolland observed as early as 1914 that tubercle bacilli, injected into the skin of prepared animals, disintegrate and that the location in which the superinfection was introduced becomes sterile. Lurie confirmed this observation in 1929. Also, according to Rich, there is no doubt about the accuracy of observations of this kind: In some cases the disappearance of the bacilli is so marked that even solitary, isolated bacilli in serial sections may be found only with extreme difficulty (Rich, l.c, p. 457).

Fig. 8. Radiographic registration of the development of experimental pulmonary infiltrations. Rabbit W. 48. Testicular preinfection with human tubercle bacilli (which are nonvirulent for rabbits); intravenous superinfection with virulent (bovine) bacilli, 21 days later.

a . . . 1st radiograph: 16 days after the superinfection, showing complete opacity. (The opaqueness began as early as 2 days after the superinfection).

b . . . 2nd radiograph: 71 days after the superinfection, displaying absolute transparency.

At this time all control animals infected intravenously were dead; they perished of generalized tuberculosis. (These experiments were performed with the collaboration of Dr. G. Weber).

1935, pointed to certain terminal changes in tuberculous lungs which appear immediately before death and can be considered as the cause of the fatal outcome. Canetti interpreted (1946) this phenomena as the consequence of an allergic inflammation: " . . . a great number of these patients are victims of allergy; however,

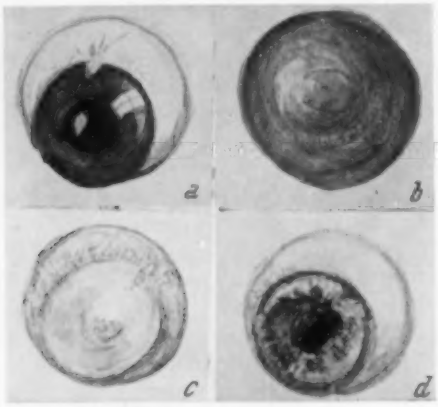

Fig. 9. *Experimental Ocular Koch's Phenomenon.*

a . . . The eye of a normal guinea pig, 3 days after infection of the anterior chamber with bovine tubercle bacilli. No more than a slight ciliary hyperemia was observed at the level of the injection.

b . . . The eye of a preinfected guinea pig, 3 days after the same treatment as given to the animal of fig. *a*. Intense conjunctival and ciliary hyperemia was present; the cornea displayed a lead-grayish opacity; the iris was covered by yellowish exudate masses.

c . . . The same eye, as demonstrated in fig. *a*, 16 days after the intraocular infection. The whole bulbus was intensely enlarged; a dense pannus covered almost the entire cornea; the center of the cornea was very cloudy. Disintegrating caseous masses permeated the ciliary body. Perforation of the bulbus was imminent.

d . . . The same eye as showed in fig. *b*, 17 days after the superinfection. The general hyperemia, regressed; the transparency of the cornea returned; only the corneal border still displayed some thin pannus. The antichamber cleared up. The iris displayed only scattered tubercle. The pupillary area still was covered by a grayish-black rind.

(These drawings were made by Dr. E. Metzger, who executed the experiments and made the observations).

this is not a true allergic death—the allergy only suppressed the last areas in which the change between blood and air could occur; the patient would survive if a little more of the lung tissue remained healthy!" Nevertheless: " . . . besides these types of cases which occur very frequently, there are some instances of authentic allergic death, which is death by shock." According to Canetti,

in such cases, the patients sometimes show no signs of an imminent catastrophe: "The general condition deteriorates brutally; a condition of shock develops, characterized by algidity and hypotension, and then death follows in a few hours."

B. *Morphological Characterization of Experimentally Produced Pathogenetic Interpretation*

From the morphological point of view, the following changes were observed in animals infected experimentally: (1) Typical, roundish granulation foci, formed by the conglomeration of histiocytes. These foci may appear without necrosis as "epithelioid cell tubercles" or as "typical tubercles" containing central necroses. Epithelioid cell tubercles are characteristic not only of the onset of a fresh exogenous, or of a newly exacerbated tuberculosis, but also of torpid processes occurring during the intervals between exacerbative episodes, and avirulent infections in general. We observed that the predominance of epithelioid cells—histiocytes—characterizes processes in which the natural or acquired resistance predominates. In these cases a conspicuous tendency to cicatrization by accumulation of connective tissue also is present. Necroses, in contrast, appear in tubercules if a virulent infection is fully effective. However, in animals properly prepared, superinfections with avirulent germs, or even with extracts of killed bacilli, also may produce large necroses (Fig. 10). Necroses are more extensive and develop more rapidly the higher the susceptibility (sensitivity) of the attacked tissues to tubercle bacilli.

(2) Intra-acinous condensations, characterized by serous, hemorrhagic, or leukocytal and alveolar-histiocytal infiltrations: These pneumonic processes also may be subjected to necrosis or may dissolve without necrotic processes. Macroscopically, the following types of infiltrates may occur: (a) inflammatory edema; (b) red pneumonic hepatization; (c) gray pneumonic hepatization; (d) gelatinous pneumonia; (e) caseous pneumonia; and (f) pneumonia of rubber-eraser consistency. Then too, in these infiltrates the predominance of histiocytes—primarily alveolar histiocytes—signifies a natural or acquired resistance, that is, the fact that genuinely avirulent germs are present (Fig. 1), or, that we deal with agents, the virulence of which was depressed either by pre-existent or by newly produced immune substances (Fig. 7); while necroses indicate that the agents could effect and develop their full virulence (Fig. 3), or that the sensitivity of the involved tissue was increased (Fig. 10). The more rapidly and extensively the development of

necroses occurred after contact with the bacilli, the greater the increase in sensitivity of the involved tissue.

Thus, considering the clinical processes and the accompanying morphological phenomena which develop in experimental infected

Fig. 10. Rabbit No. 2642. Testicular preinfection with virulent (bovine) germs. Intratracheal "superinfection" with the extract of killed tubercle bacilli 21 days later. The animal was sacrificed 8 days after the intratracheal injection. The autopsy disclosed a massive, very extensive aspiration infiltration of the left lower lobe. Large round cells ("alveolar histiocytes") of a typical desquamative (rubber eraser-like) pneumonia predominated in the condensation. However, quite extensive necroses (*n*) were also present.

Pathogenetical interpretation: The necroses developed in this case as the expression of the increased inflammatory susceptibility (hypersensitivity) induced by the preparatory testicular infection.

animals, we understand that in consequence of the increased sensitivity after inoculation with genuinely harmless avirulent agents, lethal conditions may develop, characterized by extensive necroses, just as in cases in which highly virulent infections were produced. On the other hand, due to immunity induced by a suitable prepara-

tion, the effect of virulent germs may be decreased in a measure so that clinically the healing tendency predominates and histiologically cellular infiltrates prevail, just as in infections caused by avirulent agents.

We conclude from these observations that, at any rate in animal experiments, necrosis, disintegrative processes and cavitation, even if affecting very extensive areas, indicate generally not the malignancy of the disease, but only the fact that relatively large masses of tubercle bacilli or their extracts were effective, or that a very high degree of sensitivity was present. Similarly, the manifested healing tendency of a pulmonary tuberculous lesion cannot be considered as definite proof of the benignity of the process, but only as an indication of the fact that a strong resistance was present. We know that the increase of sensitivity is a transitory phenomenon which vanishes rather quickly; similarly, the immunity which develops following a new exogenous infection, or subsequent to the reactivation of an old focus, also fades eventually.

COMMENT

In modern phthisiology "allergy", that is, increase of the natural inflammatory disposition ("hypersensitivity") and, in other cases, the decrease of the normal susceptibility ("immunity") to tubercle bacilli, became indispensable concepts. Both hypersensitivity and immunity in tuberculosis can be produced under exact experimental conditions, permitting the prediction of the probable results—anatomical changes of the organs, clinical symptoms, the course of the disease—almost definitely. There is a marked parallelism between allergic conditions and morphological phenomena in experimental tuberculosis.

To summarize briefly but schematically, in our animal experiments predominantly cellular infiltration signifies the prevalence of a strong congenital or acquired resistance; necroses and disintegrative processes indicate the effect of virulent bacilli or the influence of relatively large masses of phlogogenic living or dead specific substances; while the extension of the infiltration characterizes the degree of the sensitivity at the time of the critical spread.

Clinical conditions and pathologic-anatomical changes observed in animal experiments also occur in human pathology. *The increase of the sensitivity, as well as the increase of congenital and acquired resistance to tubercle bacilli can be recognized as factors which decisively influence the course of every tuberculous infection.*

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A CASE OF BILATERAL POST-TRAUMATIC PORENCEPHALY

A Clinico-Pathologic Study of a Microcephalic Idiot*

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Developmental disorders of the brain have attracted attention of anatomists, neurologists and neuropathologists. Among these disorders cystic degenerations of the brain appear to be very common findings. About 50 per cent of Benda's microcephalic cases showed cystic degenerations.[1, 2] A great majority of them were unilateral. Trauma was found to play a most important part, as was emphasized by Schwartz,[3] also toxic, chemical, infectious and inflammatory factors, embolism and thrombosis, which can take place in utero, at birth or after birth. The clinical pictures produced by these defects are of great interest to pediatricians and psychiatrists. Although intellectual defect is not always in direct proportion to the size of the brain or of the lesion, the degree of maldevelopment accounts for variations in clinical pictures. A case of a low grade microcephalic idiot studied until her death at 39, in whom bilateral porencephaly of the brain caused by birth injury was found, seems to be worthy of presentation.

Case M.O. #43160, the oldest of two children, was born of young, healthy parents at full term by difficult instrumental delivery. The labor was difficult and protracted and high forceps were used. The family was told that the baby had brain hemorrhage. Peculiarity of development was noticed at six months. Her head was noticeably flattened in the back. She was difficult to feed, to take care of, was very untidy, never learned to feed or dress herself, spilled her food on her dress, drooled, began to walk at three years and said a few indistinct words at five. In 1923 she was admitted to the Fernald State School at the age of six. There she was found unable to learn, to play with other children, easily excited, screamed at the top of her voice until she became hoarse, tore her clothes, struck herself on the nose and scratched her face until it bled. For two months preceding her transfer to the Boston State Hospital, she had been extremely agitated and noisy, especially at night, and assaulting the other children.

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She was admitted to B.S.H. in 1944 at the age of 27. Her mental age was one year and ten months, her I.Q. 12 per cent. She was undersized, overnourished, had an unsteady, tottering gait, held her hands stiffly in front of her as if to ward off a blow. She ground her teeth and made whispering noises. When excited she ran back and forth with fists clenched, pushing everyone out of her way. She had a great deal of pain during her menstrual periods and was more excited at that time than usual. She could not carry out simple orders, rocked in her chair for hours, did not pay any attention to questions as though she did not hear them (although her hearing was good), did not answer, but just grunted. Her facial expression was one of worry and apprehension. She was diagnosed a microcephalic idiot on the basis of developmental cranial anomalies.

Physical examination: Heart and lungs were negative. B.P. 108/78. Pupils reacted to light and distance. Deep reflexes were overactive. Gait unsteady, tottering. Kernig and Babinsky were not present. She did not have convulsions. *Laboratory data:* Hinton and Wassermann were negative. All blood tests were within normal limits. X-ray of the skull: "The skull is microcephalic. There is no evidence of increased intracranial pressure. There is a pronounced localized protrusion and thickening of the tables in the right parietal region. This appears to be a purely expansile lesion with no evidence of infiltrative or destructive changes and is attributed to a gland lesion of undetermined nature". *Mental examination:* She did not speak but made inarticulate noises, was restless, untidy and dishevelled. Her attention could not be gained. She was grimacing, spitting, talking to herself, though unintelligibly. She laughed raucously. She appeared clumsy in all her actions.

Clinical course: In 1950 she fell and sustained transverse fracture of the left clavicle. She had many falls causing bruises and lacerations. Four years later, she fell downstairs and lost consciousness. Two lumbar punctures were negative. Pupils reacted well. The eye-grounds were negative. There were no neurologic signs. It was thought that she had concussion of the brain. She had been a problem in management because of untidiness, lack of sphincter control, overactivity, destructiveness and assaultiveness. She was treated with reserpine with some little success. She developed bronchopneumonia, and died in 1956 at the age of 39.

Postmortem examination: The autopsy was performed four hours after death. The cause of death was bronchopneumonia. Except

for the brain, all the organs were well formed. The anatomical findings included passive congestion of liver and spleen, fibroid uteri, asymmetrical skull with thickening of inner tables, microcephaly, porencephaly involving right temporal, parietal and occipital lobes and internal hydrocephalus. Head was small and asymmetrical. Right parietal bone protruded more than the left forming a bossa. Right occipital bone was flattened. The scalp, in places, was firmly adherent to calvarium and reflected with great difficulty.

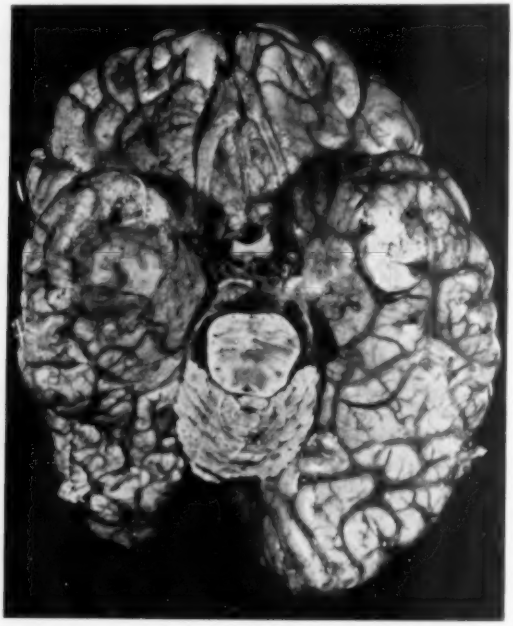

Fig. 1. The view of the base of the brain showing asymmetry of the hemispheres, retraction and smallness of the right occipital lobe as compared with the left, and the round shaped bulging of the middle of the temporal lobe.

Calvarium was firm and thick. Dura mater was adherent to calvarium. Dural sinuses were free. Pia-arachnoid appeared thin and transparent over the convexity of the gyri and thickened in the sulci. Brain weighed 680 gms., was small and asymmetrical. (Fig. 1). Right orbital area measured 4.0 cm., the left 4.7 cm. Distance

from uncus to occipital pole was 11 cm. on the right, and 12.5 cm. on the left. Convolutional pattern was grossly abnormal. The gyri were small, and specially small and firm in the right occipital area. A round bulging cyst with very thin walls, measuring 2×2 cm. protruded in the midle of the third right temporal convolution and hippocampus. The right uncus was noticeably narrowed as compared with the left. The preserved anterior part of the right temporal lobe, representing less than a third of the whole temporal lobe, had a recognizable pattern of the first, second and third gyri. The rest consisted of a thin shell forming the wall of an enormous cyst involving the right temporal lobe, the right occipital lobe, the right parietal lobule and the opercula. The surface of this shell still had recognizable gyri which were very small and narrow, flattened, firm and shrunken, as if macerated. These remnants were separated by ribbons of thin, transparent, membrane-like tissue. The posterior two thirds of the right hemisphere were much shorter than the corresponding parts of the left hemisphere and the right occipital pole formed the posterior end of this enormous cyst. The cyst wall was firmly adherent to the dura which was in turn adherent to calvarium. The horizontal section of the brain showed that it communicated with temporal and occipital horns of the right lateral ventricle, which were greatly dilated and filled with clear, colorless fluid. The right foramen of Monro was greatly dilated. The basal pia was greatly thickened and was constricting the oculomotor nerves. The optic nerves were flat and thin, the chiasma was small, flat and thin. Other cranial nerves showed no gross changes. The pons appeared small and asymmetrical, the right half more atrophic than the left. Cerebellum was well developed and showed no gross changes on sectioning. The pituitary gland was small, reddish and soft. In the medulla, the left pyramid appeared slightly smaller then the right. Spinal cord showed no gross changes.

In the horizontal sections of the brain, the first frontal gyri of both lobes were not strikingly different. The right F2 and F3 were small and only slightly narrower than the left. The right operculum and the right island of Reil all but disappeared, their place being taken by thick connective tissue membrane. The right Sylvian fissure was dilated and crossed over by connective tissue strands. The genu of the corpus callosum was negative, the splenium was very narrow. Right gyrus cinguli was very narrow and small. Right hippocampus and its fimbria were destroyed. Right occipital lobe—the calcarine fissure was identified but most of the

tissue of the area striata was shrunken and firm. Left occipital horn was dilated but not deformed. Left occipital lobe presented no striking gross abnormalities. Right occipital lobe was microgyric and sclerogyric. A very large part of the right central white matter had been destroyed, making it possible for the cyst to communicate with the right lateral ventricle. (Fig. 2).

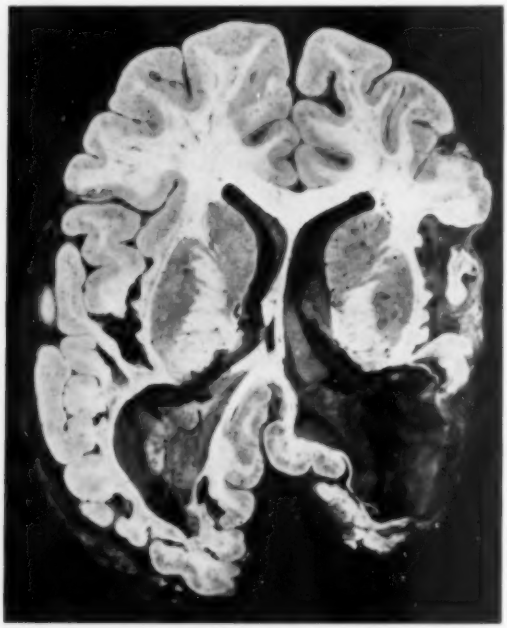

Fig. 2. Horizontal section of the brain to show a large cyst of the occipital and temporal lobes communicating with greatly dilated occipital horn of the right lateral ventricle.

The wall of the cyst was of uneven thickness, in some parts almost paper-thin. It was filled with a clear fluid and it had no partitions. There were small areas of degeneration of the gyral white matter of the right temporal and frontal gyri. The cortex of these gyri, however, was preserved enough to have the usual outline, although the gyri were very small.

There was a small cyst in the white matter of the left temporal lobe, divided by many delicate strands of tissue. It did not communicate with the left lateral ventricle. The brain did not appear

collapsed on either side. On the contrary, the right side bulged considerably.

Serial sections of the whole brain revealed differences in shape and structure of the cyst at different levels due to irregularity of its configuration and uneven thickness of its wall. (Fig.3). The

Fig. 3. Horizontal section stained with Loyez method to show bilateral porencephaly and necrotic changes of the white gyral matter of RF2 and RF3 and of the left temporal lobe.

cavity which extended from the right occipital pole to the first temporal gyrus was in direct communication with the right lateral ventricle and bulged considerably on the external surface of the right hemisphere. The lining of the inner surface of the cyst was firm, white and rather smooth. The wall of the cyst was of uneven thickness, becoming almost transparent in places. The cortex on its periphery was thin and firm.

Microscopical examination showed greatly thickened pia-arachnoid especially over the cyst wall and involved parts of the

right F2 and F3, with occasional deposits of calcium in its numerous thick fibrous meshes. The wall was lined with thick layers of glial cells and glial fibers, mostly fibrous astrocytes. Nerve cells were absent in the wall and showed all stages of involvement in surrounding gyri, from swelling to atrophy. Myelin stain showed loss of myelinated fibers. Scarlet-red stain revealed macrophages containing numerous small fat globules. The gyral white matter of right F2 and F3 was completely devoid of myelinated fibers and consisted of delicate glial mesh formed by glial fibers and containing glial cells.

Basal ganglia—right caudate nucleus showed edema and a mild loss of nerve cells. Right insula was completely destroyed and its place occupied by a conglomeration of thick glial wall, numerous vessels and delicate fibrillary meshwork.

DISCUSSION

This case of microcephalic idiot represents late consequences of birth trauma caused by prolonged labor and high forceps. The history mentions diagnosis of cerebral hemorrhage. The most striking defect was in the right hemisphere, but on closer examination of the whole brain sections, smaller cysts were seen in the gyral white matter of the right frontal lobe, F2 and F3, and in the white matter of the left hemisphere. Horizontal sections revealed a very large cavity in the central white matter of the right temporal, parietal and occipital lobes with a large part of the central white matter destroyed, making it possible for the cyst to communicate with the right lateral ventricle and several smaller cystic degenerations, both in the right and left hemisphere which did not communicate with lateral ventricles. Several theories of the mechanism of the formation of porencephalies have been proposed. According to Schwartz,[3] the terminal vein, the branch of the internal cerebral vein, is so often affected in child birth that its lesion may be considered the most characteristic of all cerebral injuries resulting from birth trauma. Lesions of the ventricular lateral vein are also frequent, affecting the cerebral area drained by this vein—the occipital white matter. The circulatory disturbances, anoxemia and stasis may develop without hemorrhage and lead to necrotic changes in the white matter and to formation of cystic degenerations. Schwartz emphasizes that symptoms of severe involvement of the central nervous system which appear during the first year of child life are caused in the great majority of cases by birth injuries, and that cystic degenera-

tions, porencephalies are caused by "a dissolution of the white matter in the area drained by terminal and lateral ventricular veins." In their study of brain defects, Yakovlev and Wadsworth[4] distinguish two groups of porencephalies; one which they called "schizencephalies" or true clefts represents true malformations, developmental faults, due to arrest of intrauterine development; the other which they named "encephaloclastic porencephaly" is the end result of necrotic softening and destruction of the cerebral wall, the condition resulting from numerous causes, such as hemorrhage, anoxemia, thrombosis, embolism, trauma, inflammatory and degenerative processes in the brain. These porencephalies may occur during the fetal life, at birth or after birth. According to this definition our case belongs to the second group, encephaloclastic porencephaly, caused by softening and disintegration of the cerebral tissue following birth trauma. The majority of cases of encephaloclastic porencephaly, described in literature, are unilateral, although a few cases of bilateral porencephaly have been described.[5,6,7] Ours is a case of bilateral encephaloclastic porencephaly, more pronounced on the right than on the left. This severe loss of white matter and sclerogyria of the cortex accounts for severe disturbance of mentation, idiocy, in our patient. She did not have convulsions, although this is a common result of cystic degeneration of the brain, covered as it is with thickened adherent pia-arachnoid. Treatment of convulsions by surgical means was advocated by Patten[8], and prevention of birth traumas were discussed at length by Schwartz.[3]

SUMMARY

A case of bilateral porencephaly resulting from birth trauma is presented and its clinical and pathological features discussed.

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FURADANTIN® A COCCIDIOIDAL FUNGICIDE

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At the coccidioidal symposium sponsored by the United States Department of Health, Education, and Welfare at Phoenix, Arizona in February 1957, I mentioned a drug called N.F.-254, a nitrofufural drug which showed excellent in vitro studies, but in vivo studies proved too drastic for the central nervous system (1). However, since that time, other furacin-like drugs have been introduced. The new furadantin drug, Nitrofurantoin [N-(5-nitro-2-fufurylidene)-1-aminohydantoin] may prove of use as it can be given both intravenously and orally in other bacterial infections.

Employing ampoules of intravenous Furadantin® purchased on the open market, various dilutions into Sabaroud's media were incorporated in Petri dishes and using plain Sabaroud's for controls, then streaked the plates with loopfuls of pus from a severely disseminated coccidioidal case.

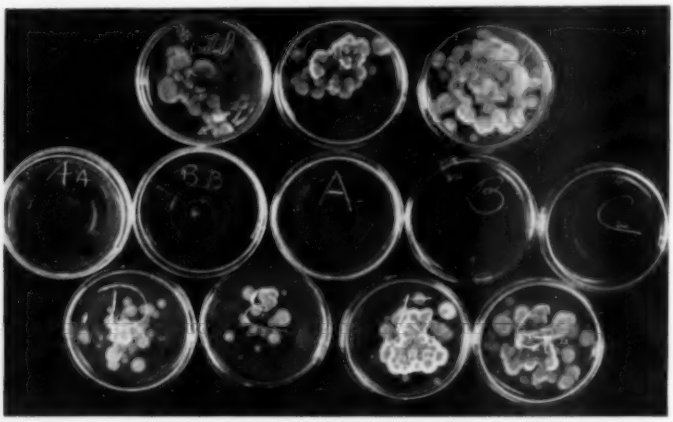

Fig. 1. Three upper Petri dishes with growing cultures are the controls. Five plates showing no growth to 300 micrograms per milliliter. Return of growth seen from 150 micrograms per milliliter through 75, 30 and 15 micrograms per milliliter.

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For four weeks, the Petri dishes were sealed with scotch tape and set at room temperatures. The results are as follows:

3000 micrograms per milliliter showed no growth
1800 micrograms per milliliter showed no growth
1200 micrograms per milliliter showed no growth
600 micrograms per milliliter showed no growth
300 micrograms per milliliter showed no growth
150 micrograms per milliliter showed colony growth
75, 30 and 15 micrograms per milliliter showed definite colony growth.

All the controls grew profusely as expected, and began to show growth within 72 hours.

The safety of this drug has been demonstrated in other fields if instructions for use are followed. The next step is clinical trials.

CONCLUSIONS

Furadantin® completely inhibits the growth of coccidioides immitis in vitro at 300 micrograms per milliliter. Because it has been used in another field it may be safely tried in the field of coccidioides and may offer some hope. Further study is necessary.

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AN INFANT HYGIENE CAMPAIGN OF THE SECOND CENTURY.*

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Much has been written concerning the degeneracy of Roman civilization and the brutal indifference displayed by the civilized, but not humanized, nations of antiquity in their treatment of the newborn. There is abundant evidence in Roman literature of the prevalence of the custom of exposure of infants and of abandonment and infanticide. Plautus and Terence made merry with this theme in more than one comedy, and many of the "modern" cynical quips on matrimony unquestionably have come down from the later days of the Roman Republic when, as Seneca says, "some women reckoned their years by their husbands." And yet—there is another side to this story of which we have heard very little—the side which deals with the efforts made by thoughtful men and women of that day to put an end to practices which they realized must eventually sap the foundations of national virility and which in the second century A. D. crystallized into what seems to this writer, at least, as a more than sporadic effort to teach the lessons of infant hygiene to the general public.

We learned in our primary schools that the legendary Romulus was himself an exposed infant who had been suckled by a wolf. To increase his warlike subjects when he became ruler he obliged his people to bring up all male children, except those deformed and crippled, and also the first born of all females. But there was also a human note in this decree, for even the crippled could not be exposed unless 5 neighbors gave approval.

The word proletariat, so much used nowadays, had a specific application in its original meaning: the *proletariat* consisted of citizens who had no property, but who were valuable to the State through the children which they produced. In the Rome of Augustus, corruption of morals, with the consequent inroads upon the legitimate population of the great world-metropolis, caused that astute ruler to give early attention to legislation regulating marriage and celibacy—the "*lex Julia et Papia.*" In the old Rome of the *patria protestas*, the father had the power of life or death

*Read before the American Child Hygiene Association at the Tenth Annual Meeting in Asheville, N. C., Nov. 11-13, 1919.

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over his children; now, however, the mere possession or non-possession of offspring determined a man's legal rights. A married man with no children could only take half of an inheritance. In the holding of certain offices the candidate who had the most children was given preference. All personal taxes were remitted to Roman citizens who had 3 children. Citizens who lived in Italy enjoyed this privilege if they had 4 children and those who lived in the provinces if they had 5.[1]

These laws remained at least partly in force, despite the changes of Caracalla and Constantine, until their abrogation by Justinian. Augustus also set aside a reward of 2000 sesterces (about $40.00) for anybody who would bring up an orphan. From the death of Augustus, 14 A. D., to the accession of Nerva, 96 A. D., little social progress obtained amidst the political and military turmoil of Rome. But from the time of Nerva to the passing of the Antonine Emperors, such advances were made as to emphatically warrant the assumption that child welfare of a primitive kind was being propagated in Rome during the second century. Nerva tried to put a stop to infant abandonment by having the State subsidize poor parents (97 A. D.). Three years later, 5000 children were receiving state aid. A coin shows the emperor seated in a chair dispensing charity to a boy and girl, with the inscription, "*Tutela Italia.*" Trajan loaned money to land owners, the interest of which was used to support parentless or abandoned children.

Hadrian, who had Plutarch as a master and Suetonius for a secretary, and who was himself a tremendous student and a great traveler, might be expected to have enlightened and liberal views in spite of his imperial absolutism. "Here in the second century we see an emperor," Duruy says, "employing logic in the service of humanity." For he ruled that any woman who had been free at the time of pregnancy must as a result give birth to a free child. Women were allowed to make wills and inherit rights in the property of sons who died intestate. Carthaginian priests had been forbidden by Tiberius to offer children in sacrifice to Moloch; this law was repeated and enforced by Hadrian.

The right of the Roman father to kill his own son was abrogated—Hadrian banishing a father who had done this. The reign of law as interpreted by jurists began with this emperor.

Antonius Pius extended throughout Italy the loan system of

[1] "The Child in Human Progress," G. H. Paine, New York, 1916, pp. 227, et seq.

Nerva, the large income derived therefrom being devoted to the care of abandoned children. An institution for the care of female orphans, heretofore exposed without scruple, was founded in honor of his wife Faustina, the *"puellae alimentariae Faustinae."* A medal shows on one side Faustina and on the obverse Antonius surrounded by children and inscribed "Puellae Faustinae."[2]

This work was continued and amplified by the great philosophic emperor, Marcus Aurelius. But not only were these passive measures employed to prevent destruction of child life, but books were written bearing on the problems of the care of the child and the importance of rearing healthy offspring—to spread the propaganda of infant care.

It was during the reign of Trajan, between 110 A. D. and 130 A. D., that Rome became the home of the greatest obstetrician and pediatrician of antiquity—Soranus of Ephesus. This wonderful physician was the most illustrious of the school of Methodists, founded by Asklepiades—but he was too great to be bounded by the limitations of any narrow cult. He was probably educated in Alexandria, but he came from a highly civilized region of Asia Minor which had flourished under Grecian influences for many generations, although today little remains but a memory of the name of its beautiful city—Ephesus. The obstetrics of that day was practiced by midwives, usually slaves. In difficult or important cases, the physician was called. In the work of Soranus, it is obvious that the directions for the care of the child were written for use by the nurse or the mother, and that this was to a certain degree a popular treatise similar to the "baby books" of today. Translations and commentaries on Soranus have been made in Latin, German and Russian; Lieutenant Colonel Fielding Garrison, in an abstract not as yet published, was probably the first to summarize the pediatrics of the Ephesian physician in English.

At the XI International Medical Congress in Rome, (1895), I. V. Troitski, writing in Russian, compared in parallel columns the practice of Soranus of the second century with the teachings of authorities of the late nineteenth century, an interesting document, which, through the assistance of Mr. J. H. Ohsol, of Washington, I am enabled to study carefully.[3]

Anyone who examines Soranus's work on pediatrics, even without its commentaries, will scarcely doubt that the Roman

[2] Ibid I, p. 248.
[3] Soranus Ephesius," I. C. Troitski, Kiev, 1895. (In Russian).

physician wrote the most modern work on infant nursing that appeared up to a century ago. The changes in modern nursing care would be surprisingly few, if we excluded the innovations due to our knowledge of antiseptics, while the practical instruction is so sound, that with some editing and the abandonment of swaddling and wet nursing, Soranus's textbook could be used in the education of the nurse or mother certainly to greater advantage than any work of a similar kind written up to the time of Underwood.

Beginning with the twenty-sixth chapter of his book,[4] Soranus tells how to determine the strength and vitality of the newborn, by its cry and its appearance. The method of tying the umbilical cord is next considered. He shows splendid surgical sense in his directions, warning against the use of dull instruments and lacerating methods. He tells how to care for the skin of the newborn, and dismisses several faulty methods of the past. Swaddling he thinks necessary to keep the infant's limbs straight, yet he cautions against certain vicious practices in connection with this custom, gives each procedure in great detail, and insists on cleanliness. The bedding and bedroom of the newborn next claim his attention, and he insists on a soft mattress filled with grass or linden fluff, again frequent changes of clothing and absence of bad odors.

The feeding of the infant forms an extensive chapter. Soranus declaims against giving foreign food to the newborn. No food is needed for 3 days, he says. Possibly a little honey may be given with water, but nothing else. As most of the obstetrics of that day was performed by midwives there was much hemorrhage and many infections in childbirth. "Milk under these conditions is bad," says Soranus, "so it is best to secure a wet nurse for the first few weeks." He believes in wet nurses—"it saves the mother for future childbearing," he says, "and also saves her beauty." Slaves were most frequently used for this purpose. Soranus does not say that wet-nursing is the best practice—but that it is the most expedient. Of course only the wealthy employed physicians and only the very wealthy an obstetrician. Soranus unquestionably had a wealthy clientele, for he advises not one wet nurse, but 2 or 3, in case one should be taken ill.

He tells very explicitly what kind of a woman to choose as a wet nurse, how she should qualify physically and mentally,

[4] "Sorani Gynaeciorum," ed. Valentine Rose, pp. 248, 292 cap. XXVI—XLII, Greek text, Liepsic, 1882.

"The essential mental qualities of a good nurse," he says, "are patience, common sense, good nature or gentleness and neatness." No one before or since has written more intelligently or more exhaustively on this subject.

To judge of the quality of the nurse's milk he gives several tests. "Do not judge the milk simply by a poor appearance of the infant," he says, "for the milk may be of the best, and the infant have some disease which prevents proper nutrition." To test the milk he gives information as to its proper color, its odor, its consistency. Its density is established by mixing it with water and observing its behavior. He describes the taste of normal human milk and how it should act when exposed to the air. Its behavior when shaken, and the appearance and persistence of air bubbles furnishes another index to its density. Also when a drop of milk is placed on the finger nail it should not run off quickly, nor change its shape when the finger is shaken moderately, but it should do so when the hand is shaken rapidly. "When milk proves satisfactory under these tests, even when the mother is not on a proper diet, it is very good milk," says Soranus. Crude as these tests were, they were valuable, and practical, and showed what a careful, reasonable observer Soranus must have been.

He not only prescribed a rational diet for the nursing woman, but also special exercises. The influence of indigestion on the quality of milk is known and emphasized by him. He warns against excessive use of wine by the nurse, and dissipation, generally, he condemns. The technic of breast feeding is next taken up, conditions when the nurse should not nurse the child, the proper position for nurse and infant, etc. "Feeding at irregular intervals and often during the day and especially during the night may be the cause of sickness in the infant." Soranus emphasizes this by saying that the infant should never be nursed to satiation, nor should the nurse sleep with the infant nor allow the infant to sleep while at the breast. Moderate crying is helpful to the infant as exercise. "Crying," he says, "is not caused by hunger alone. An inconvenient position, pressure of the clothing, irritation of the skin, too much food, excessive heat, colic, and various diseases may cause crying." He then tells with great patience how to differentiate between the various causes. We have read this same material in our "modern" baby books; it has changed very little.

"Be careful not to move or swing the baby after feeding it—or you will have vomiting," he says; "and if the baby crys after

feeding it, do not threaten it or yell at it; caress it, amuse it. Fear is bad for infants."

To increase the quality and quantity of milk he advises a careful examination of the nurse to see if any disease is present. If none is discovered, then the watery milk may be improved by eating concentrated foods such as eggs, goat's milk, flour meal, etc., and drinking less water. Light exercise, singing, discus throwing, deep breathing and massage are also recommended. "All medicines and popular remedies used to increase the quality of milk produced injure the stomach and the digestion of the nurse," he says; continuing, "the use of such medicines is simply injurious."

To correct heavy milk he prescribes baths, lighter food and more liquids.

He tells in great detail how to bathe and clothe the infant. To atone for the inactivity produced by swaddling, Soranus gives a complete system of massage and passive movements, which exercise the infant's muscles. In all of these he is striving to prevent asymmetrical development and deformities of the limbs.

How to care for the umbilical cord, to prevent hernia, when and how to discontinue swaddling, how to teach the baby to sit up and walk, and when and how to wean, are among the things he writes about. He warns against the premature use of starchy foods—"nothing but milk should be given up to the sixth month." Honey is first allowed, later barley soup, then gruel from parched grain, last of all eggs. The change to more solid foods is permissible at 1½ or 2 years. The infant should preferably be weaned in the spring—never in the summer. Partial breast feeding may be continued for 1½ to 2 years.

The fat infant should be given less food; the thin one, more nourishing food. He discusses rational methods of curbing the tendency of some children to overeat and of inducing others, with poor appetites, to eat enough. "If a child becomes ill during weaning," he says "stop weaning at once."

The eruption of teeth is written of briefly. The gums must not be pressed on or bruised at this time. The nurse also should modify her milk by taking less solid food and more water.

Nothing written up to the late eighteenth century has equaled the work of this physician of 1800 years ago in clearness, in sound hygienic sense and in independence of thought. This will be all the more remarkable if we remember that he wrote on a subject that is even today overgrown with unsound tradition.

Soranus did not emphasize but rather approved the custom long established in both Greece and Rome of allowing infants to be nursed by wet nurses rather than their mothers. This course was to him, perhaps, the path of least resistence. He was a Greek and many of the ethnic arguments used later by Gellius did not occur to him. It was better to have infants nursed by healthy slaves than by dissipated mothers—that was probably his real meaning when he said wet-nursing was "more expedient" than maternal feeding.

History cannot trace Soranus after the year 130 A. D. In that same year, Aulus Gellius, noted later as a Roman lawyer and literateur, was born. Gellius spent some time in Greece, and returning to Rome published his *Noctes Atticae*, a series of discourses on language, literature, history, sociology and many other things. The Emperor Antonius Pius, whose reign began in 138 A. D., inaugurated an unprecedented era of peace and happiness in Rome. Conditions were favorable for the diffusion of knowledge and the spread of ideas relating to public welfare, and to the growth of altruism. So when the Greek philosopher Favorinus speaks in the pages of Gellius, he is undoubtedly voicing a positive sentiment concerning the custom of wet nursing that had been growing up in Greece as well as in Rome, in marked contrast to what was believed and practiced even in the time of Soranus. Strangely enough, this speech of a legendary Greek philosopher left a far deeper impress on the later medical literature than the splendid treatise of the historical Greek physician—perhaps because the metaphysical style and emperical method of Gellius appealed more strongly than Soranus' rational aphorisms, to the post-medieval mind. The didactic poem, *La Balia*, written about 1560 by Luigo Tansillo, was a metrical setting in Italian of this essay.[5] The same theories were set forth in Scaevole de St. Marthe's Latin didactic poem, "Paedotrophia," published in 1584.[6] In fact its influence can be seen in most of the early writers on nursing—Bagellardo being one of the very first. Omnibus Ferrarius, of Verona (1577), quotes the lambs and goats-wool incident, as also does John Peachey in his treatise on infant feeding (London, 1596). Jacques Guilleman (1609) says "the mother who nurses her own infant is the complete mother," almost the exact quotation of Gellius.[7] Van Swieten's "Aphorisms of Boer-

[5] "The Nurse," a poem, translated from the Italian of Luigo Tansillo, by William Rosco, Liverpool, London, 1798.
[6] "Paedotrophia," translated from the Latin of Scaevole de St. Marthe, by H. W. Tytler, M.D., London, 1797.
[7] "Some Seventeenth Century Writings on Diseases of Children," G. Still, in Osler Anniversary Volume, New York, 1919.

have" also shows its influence.[8] In spite of its praiseworthy purpose and its undoubted influence, the essay was very defective in its physiology. Perhaps it made even better propaganda because of that, but it is not true that milk is simply blood turned white, nor are mental and physical characteristics transmitted by maternal milk. Thus have the microscope and the test tube shattered many a picturesque belief. The disregard shown by the great philosophers, Plato and Aristotle, to the rights of the living child is in marked contrast to the stand of Favorinus on the question of the destruction of the embryo "while it is still in the hands of its artificer nature," which he characterizes a practice "deserving of public detestation and abhorrence." This would seem a strange doctrine for that day—yet it is simply another evidence of a changed sentiment of thinking men and women in their attitude toward the child.

The following is a translation of the Gellius essay, a familiar work to all students of Latin literature:

"*Dissertation of the philosopher Favorinus in which he induced a lady of rank to suckle her child herself, and not to employ nurses.*"[9]

"Word was brought to Favorinus, the philosopher, when I was with him, that the wife of one of his disciples had been confined and a son was added to the family of his pupil. 'Let us go,' he said, 'to see the woman and congratulate the father.' The father was a senator and of noble family. All of us who were present, followed him to the house and entered with him. As soon as he had entered, embracing and congratulating the father, he sat down and inquired whether the labor had been long and painful. When he was informed that the young mother, overcome with fatigue, had gone to sleep he began to converse more at ease. 'I have no doubt,' he remarked, 'but that she will suckle her son herself.'

"But when the mother of the lady said that she must spare her daughter and find nurses for the child, that to the pains of childbirth might not be added the toilsome and difficult task of suckling the infant, he replied: 'I entreat you, madam, to allow her to be the sole and entire mother of her own son. For how unnatural it is, how imperfect and half motherly only, to bring

[8] "The Commentaries on the Aphorisms of Herman Boerhave," Van Swieten, translated by Kapton and others, Edinburg, 1776.

[9] Noctes Atticae, Aulus Gellius, Lib. xii Cap. i. See also translation by Beloe, London, 1797.

forth a child and instantly send him away; to nourish in her own womb, with her own blood, something which she has never seen and then to refuse to support with her own milk the object which she now sees, endowed with life and human attributes, imploring the tender care of a mother.'

"'And do you suppose,' he continued, 'that nature has given bosoms to women only to add to their beauty—more for the sake of ornament than for the purpose of nourishing children. Because some women believe this (and may this be far from you), they unnaturally endeavor to dry up and extinguish that sacred fountain of the body, the natural nourishment of man, with great hazard, turning and corrupting the channel of their milk, lest it should render the distinction of their beauty less marked.

"'They do this with the same insensibility as those who endeavor by the use of quack medicines and in other ways to destroy their conceptions, lest the same should injure their persons and their figures. Since the destruction of a human being in its first formation, while he is still in the hands of his artificer nature, receiving life itself, is deserving of public detestation and abhorrence, how much more so must it be to deprive a child of its proper, its accustomed and congenial nutriment when at last it is perfected and produced to the world? It will be said, perhaps, that this omission is of no consequence provided it be nourished and kept alive by human milk, whoever may nurse it. Why does not he who says this, if he be so ignorant of nature's workings, suppose likewise, that it is of no consequence from what body or from what blood a human being is formed and put together? Is not that which is now in the breasts the blood of the mother which has become white in color by much spirit and warmth—indeed the same that was in the womb? And is not the wisdom of nature apparent also in this—that as soon as this blood, which is the artificer, has formed the new human body within its penetralia, it rises into the upper parts and is ready to cherish the first particles of life and light, supplying known and familiar food to the newborn infants? Wherefore it is believed with reason, that as the power and quantity of the parent cells avail to form likenesses of the body and mind, in the same degree also the nature and properties of the milk are potent toward effecting the same purpose. Nor is this confined to the human race; it is also observed in beasts. For if kids are brought up by the milk of sheep, or lambs with goats, it is plain by experience that in the former is produced a harsher sort of wool, in the latter a softer species of

hair. So in trees and in corn, their strength and vigor is great in proportion to the quality of the soil and moisture which nourish them, rather than of the seed which is put in the ground. Thus you often see a young and flourishing tree when transplanted die away from the inferior quality of the soil. What can be the reason, then, I ask you, that you should corrupt the dignity of a newborn human being formed in body and mind from principles of distinguished excellence, by the foreign and degenerate nourishment of another's milk? Particularly if she whom you hire for the purpose of supplying the milk be a slave, or of servile condition, or, as often happens, of a foreign or barbarous nation, or if she be dishonest, or ugly, or unchaste, or drunken; for often, without hesitation, anyone is hired who happens to have milk when wanted. And shall we then suffer our own child to be polluted with a pernicious contagion, and to inhale into its body and mind a spirit drawn from a body and mind of the worst nature? This, no doubt, is the cause of what we so often wonder at, that the children of chaste women often turn out unlike their parents, being different both in body and mind. Wisely and skillfully has our poet Virgil (4th Aeneid—V 367) spoken in imitation of Homer's lines:

> 'Sure Peleus ne'er begat a son like thee
> Nor Thetis gave thee birth; the azure sea
> Produced thee, or the flinty rocks alone,
> Were the fierce parents of so fierce a son.'

"'He charges him not only upon the circumstances of his birth, but his subsequent education, which he has called fierce and savage. Virgil to the Homeric description has added these words:

> 'And fierce Hyrcanian tigers gave thee suck.'

"'Undoubtedly in forming the manners, the nature of the milk takes in a great measure the disposition of the person who supplies it, and then forms from the seed of the father, and the person and spirit of the mother, the infant offspring. And, besides, who can consider it a matter to be treated with negligence or contempt that while they desert their own offspring, driving it from themselves and committing it for nourishment to the care of others, they cut off, or at least loosen and relax, that mental obligation, that tie of affection, by which nature binds parents to their children? When a child is removed from its mother and given to a stranger the energy of maternal fondness is checked little by little, and all the vehemence of impatient solicitude is put to silence. And it becomes much more easy to forget a child which

is put out to nurse than one of which death has deprived us. Moreover, the natural affection of a child, its fondness, its familiarity, is directed to that object only from which it receives its nourishment, and as a consequence (as in the case of infants exposed at birth), the child having no knowledge of its mother, does not regret her loss.

" 'Having by this destroyed the foundations of natural affection, however, children thus brought up may seem to love their father or mother, that regard of theirs is not natural but the result of civil obligation and social opinion.

"These sentiments, which I heard Favorinus deliver in Greek, I have related so far as I could for the sake of their common utility. But the elegancies, the copiousness and the flow of his words could hardly be arrived by any power of Roman eloquence —least of all by any which I possess."

When this was written, the Emperor Antonius Pius was in power and was destined to be succeeded by Antoninus Marcus Aurelius. There can be little doubt that during these years, which have been characterized as the happiest for children in the history of ancient Rome, the gentle and humanitarian trend of the Stoic philosophy, diffused and inculcated by the Antonine Emperors, had done much to spread the germinal ideas of such pioneers as Soranus and Aulus Gellius. A campaign for infant hygiene, small in its beginnings, was in the making, though its immediate and even remote effects were soon to be swept away in the bloody days that stretched from the end of the reign of Marcus Aurelius to the accession of Septimus Severus.

Book Reviews

Edited by

MICHAEL A. BRESCIA, M.D., NEW YORK

HEALTH AND MEDICAL CARE IN NEW YORK CITY—A Report by the Committee for the Special Research Project in the Health Insurance Plan of Greater New York. Cloth. Pp. 275. Price $7.50. Cambridge, Mass.: Harvard University Press, 1957.

"Health and Medical Care in New York City" published for the Commonwealth Fund by the Harvard University Press is a herculean accomplishment, taking almost six years, at a cost of $352,400.00 equally sustained by the Commonwealth Fund and the Rockefeller Foundation. It attempts to judge the contributions made by the Health Insurance Plan of Greater New York (HIP) to the health of the community.

For the reader who is not acquainted with HIP, it is an insurance plan which offers comprehensive prepaid medical care provided by affiliated medical groups throughout New York City. The physicians participating are paid on a per capita, profit-sharing or salaried basis, the amount of services notwithstanding. The subscribers to this plan are restricted to physicians affiliated with their group.

For the past 25 years the cost of medical care has been 4 per cent to 5 per cent of the total income. This figure is substantially less than that spent for tobacco and liquor. HIP was born after the late Mayor LaGuardia of New York City appointed a committee to investigate the problem of the people of the City to meet the costs of medical care. The employers of the City of New York and other large employee groups now had available a comprehensive prepaid medical plan, partially or wholly paid for by the City (taxpayer), employer or union. In the case of the City, as the employer, there is no choice of plan. It is HIP to the exclusion of all other insurance plans.

Only an irresponsible critic could deny that HIP does not offer all it claims, that is, comprehensive prepaid medical care with reasonable exclusions consistant with good insurance practices. The premium rates are fair and affiliated groups and individuals must conform to the high standards set by the HIP Medical Control Board. Preventive services are included. Family physicians

have access to unlimited x-ray and laboratory services and consultations with specialists are available, all at no additional charge to the subscriber. This appears, at first glance, to be a great contribution to the health of the community. In a recent appeal to the New York City Board of Estimate for a free choice between HIP and other health insurance plans, the High School Teachers Association offered complaints against HIP.

I must observe that nowhere in this volume is there an attempt to determine the degree of satisfaction of HIP subscribers.

It is regrettable that the conference of experts (from HIP, the Commonwealth Fund, and elsewhere) after a three day deliberation on purposes and methodology of this survey, did not find it appropriate to compare HIP with, for example, an indemnity type of insurance coverage. Instead, a household survey was made which included both HIP families and families in New York City not enrolled in HIP.

Some of the more interesting conclusions reached are as follows: 56 per cent of persons in the general population have some form of medical care insurance; 42 per cent of the 56 per cent have hospital care only, the rate of physician contacts was 22 per cent higher for HIP enrollees than for persons in the New York City sample, for persons 25 years of age and over in both the HIP and NYC population. Those who had the most schooling showed the highest rates of physician contact—50 per cent of 942 families in the general population with children under one year had a pediatrician, while 90 per cent of 622 HIP families were in receipt of care by a pediatrician for children under one year of age.

Further observations made it quite clear that acute non-disabling illnesses were more frequent in the HIP sample than the NYC sample, and days lost by persons in the labor force because of acute disabling conditions were greater for the HIP sample than for the NYC sample. Persons in HIP have changed their standards so that they define illness differently from those not in the Plan, giving greater weight to relatively less severe conditions. The higher frequency of illness reported in the HIP sample might be accounted for by the fact that a higher proportion of these conditions were seen by a doctor and were, therefore, more likely to be remembered than the NYC sample. Factors other than purely economic ones influenced the amount of illness reported inasmuch as the frequency of illness varied directly with increasing education of the household.

The "other than economic" was italicized, a rare occurrance in this publication. It is not difficult for this reviewer to speculate as to why the economic factors were lightly dismissed by the authors. To do so is ludicrous. It is contrary to everything known about human nature. The folly of HIP or any comprehensive prepaid scheme is obvious. A chapter was devoted to the frequency, duration, and place of hospitalization, in the two samples in 1951. There was no appreciable difference in the frequency or duration of hospitalization. However, a higher proportion of persons in the NYC sample was hospitalized in municipal hospitals and a higher proportion of persons in the HIP sample entered proprietary hospitals. No explanations were offered by the authors. To this reviewer it is obvious—economic! The HIP population all have Blue Cross coverage.

The last two chapters concerned itself with Dental Care and preventive health services. The survey indicates that more persons in the HIP population were receiving dental care. No explanations were offered. This reviewer would again assume that the difference was economic.

The survey described HIP as urging subscribers to use their privileges for preventive health care and presented evidence alleging that the HIP enrollers were receiving more health care and guidance than were their counterpart in the general population.

An excellent appendix and index occupied the remaining portions of the publication.

Just what contribution HIP has made to the health of NYC cannot be categorically stated on the basis of the facts presented in this report. No one seems to know just what plan could best serve the health needs of a community. But the consensus of organized medicine is firmly convinced that HIP or any similar plan cannot do the job, if it does not give the patient a completely free choice of who is to guide his health destinies and maintain a fee-for-service principle.

It was most unfortunate that the Commonwealth Fund and the Rockefeller Foundation did not have the wisdom to finance a study to find such a plan. A study of all medical insurance plans in New York State is about to be undertaken by Columbia University. Commonwealth Fund and the Rockefeller Foundation, please take notice!

M. KAPLAN, M.D.

SCHUTZIMPFUNGEN. Edited by Heinz Spiess. Cloth. Pp. 356. Price $13.35. Stuttgart, Germany: George Thieme, 1958.

A number of investigators from various fields interested in problems of active and passive immunization have contributed to this important book. Workers in the fields of Pediatrics, Public Health, Hygiene and Veterinary Medicine are found among the co-authors. They have accumulated an impressive wealth of material about indications and contra-indications as well as side effects of routine immunizations against many contagious diseases including diphtheria, tetanus, pertussis, poliomyelitis and small pox. The individual chapters contain valuable material on the scientific basis and methods of immunization as well as preparation and standardization of various vaccines. The bibliographies are adequate and summaries are attached to each chapter. The book will enable the German reader to become familiar with some of the latest American publications on the subject. He will also find the section on State and Immunization of interest. The compilation of this clinical and experimental material will be of aid to the practicing physicians as well as research workers in this field.

M. WEICHSEL, M.D.

THE MANAGEMENT OF CHILDHOOD ASTHMA. By Frederic Speer, M.D. Cloth. Pp. 116. Illustrated. Springfield, Ill.: Charles C. Thomas, 1958.

The author is to be congratulated on presenting such a difficult subject so succinctly. In this manual the author discusses, in outline form and most concisely, the diagnosis, etiology and treatment of asthma, focusing particular attention on the acute attack. In handling the acute attack, he emphasizes that the most important sedative is the calm and reassuring approach of the attending physician. In this regard the author quotes Urbach as follows: "The asthma doctor must and dare not forget that his own quiet, deliberate and reassuring manner and his absolute conviction that almost all cases of asthma can be cured, constitute one of the most important prerequisites for success." The tendency of late has been to place the onus of any malady or aberration, be it mental or physical, on the parents. This has been done in a most deprecating manner creating or increasing any guilt feelings on the part of the parents. It was, therefore, most gratifying to note that the author thoughtfully dedicated his book to the mother of the asthmatic child.—"It is one of the wonders of pediatric allergy practice that the mother of the asthmatic child is typically patient, devoted, observant and wise." This text is very practical and is of value to the medical student, to the practitioners and pediatricians whose forte is not allergy.

M.A.B.

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Berenberg, W. and Kevy, S.: Acute Epiglottis in Childhood. A Serious Emergency, Readily Recognized at the Bedside. (New England Journal of Medicine, 258:870, May 1, 1958).

Acute epiglottis is a serious and often fatal condition that, although infrequently recognized, lends itself to accurate bedside diagnosis with consequent institution of specific life-saving therapy. Its recognition and management should become familiar to all concerned with the care of sick children. Of the 39 cases reported by the authors, 39 had difficulty in breathing; 32 had sore throat; 30 suffered stridor; 25 dysphagia; 22 limpness; 18 irritability and restlessness; 16 drooling; 15 croupy crow; 12 cough; 12 hoarseness; 3 aphonia and 3 wheezing. Examination of the 39 patients showed that all had some degree of swelling of the epiglottis, 33 had restriction on inspiration, 25 redness of pharynx, 24 diminished breath sounds, 23 cyanosis, 20 had excessive mucus in the posterior pharynx, 12 were in shock and 3 had cervical adenitis. This study re-emphasizes the importance of H. influenzae, Group B, as the predominant but not the only micro-organism producing this clinical picture, and the life-saving value of tracheotomy to relieve the rapidly developing obstruction of the upper airway. M.A.B.

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1. Kaessler, H. W.: Arch. Ped. 74:47 (Feb.) 1957.
2. Kahan, H. *et al.*: Arch. Ped. 73:125 (Apr.) 1956.
3. Editorial: J.A.M.A. 165:254 (Sept. 21) 1957.

MEDICATED

'Baby Silicare'

POWDER AND LOTION

active ingredients:
glyoxyl diureide
dimethylpolysiloxane
hexachlorophene

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